REMARKS

Claims 2, 4, 10-11 and new claims 13-14 are currently pending in the application. Claims 1 and 6-9 were canceled in a previous paper. Claims 3, 5 and 12 are canceled herein. Claims 2, 4, and 10-11 are amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added. New claim 13 is supported by the specification at page 4, lines 22-25. New claim 14 is supported at page 5, lines 6-7. New claims 15 and 16, which recite a method for assessing the genitourinary health of a patient (claim 15) and use of the method in conjunction with other tests (claim 16), are supported by the specification, particularly at page 6, lines 9-11 ("The test can be used in conjunction with other tests to diagnose TCCB, prostate cancer and urinary infection."), page 7, lines 12-14 ("there is a blood test for cancer so this would have to be carried out on positive patients along with a check for infection."), page 7, lines 19-24 ("The test could be used as a general screen for health in the genitourinary area since it might pick up silent bladder and prostate tumours and infection - a positive test could lead to other tests to rule these possibilities out."), page 9, lines 1-2 ("The test of the present invention may be used alone or together with any other suitable test."), page 9, lines 13-17 ("... it was found that 57% of the urinary infection patients tested positive for the 37kDa fragment. This was to be expected, as EGFR over expression has been associated with inflammation and chronic irritation..."), and page 9, lines 21-28 ("... the test could be used to determine whether or not a patient requires cytoscopy..."). New claims 17 and 18 recite claims limitations that already exist in claims 4, 13 and 14. New claim 19 recites the same subject matter as claims 15, 16 and 17, but is written in independent form. The new claims therefore introduce no new matter.

Applicants also respectfully submit that there are no new grounds for search, as the Examiner has already conducted a search on the claim elements recited in the new and amended claims. The base subject matter claimed, a method for detecting the presence of a 37 kDa fragment of EGFR in the urine sample using an antibody that specifically binds the 37 kDa EGFR fragment, has already been searched and examined. The method is novel, as is discussed below. The amendments and new claims also claim this base subject matter, with additional limitations that are taken from the claims as originally filed, or add further limitations to subject

matter recited in the claims as originally filed. There is therefore no need for additional search or examination.

Claim Objections

Claim 11 is objected to under 37 C.F.R. § 1.75(c) as being in improper form as a multiple dependent claim dependent on another multiple dependent claim.

Claim 11 has been amended to depend from claim 10. Applicants respectfully request that the rejection on this basis be reconsidered and withdrawn.

Claim 4 is objected to for reciting the phrase "available from Oncogene Science, Inc." The claim has been amended to recite instead that the antibody instead is one that has been raised against a peptide corresponding to amino acid residues 1005 to 1016 of EGFR. This is supported in the specification, at page 4, lines 22-25. Applicants respectfully requests that the rejection on this basis be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 101

Claims 5 and 12 are rejected under 35 U.S.C. § 101 because they recite a "use", without setting forth any steps involved in the process, and are therefore not proper process claims under 35 U.S.C. § 101.

Applicants have canceled claims 5 and 12, thereby rendering the rejection moot.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 2-4 and 10 have been rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps.

Claims 2-4 and 10 have been amended to recite step of detection of the fragment in a patient sample and correlation of detection of the fragment to a diagnosis of bladder cancer. The amendments are supported by the specification, *e.g.*, at page 4, lines 9-14, and Experiment 1 (*e.g.*, page 5, lines 13-26). Applicants respectfully request that the rejection on this basis be reconsidered and withdrawn.

Claims 5 and 12 are rejected under 35 U.S.C. § 112, second paragraph. Applicants have canceled claims 5 and 12, thereby rendering the rejection moot.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 2-3 and 10 are rejected under 35 U.S.C. § 112, first paragraph, the Office Action stating that the specification does not reasonably provide enablement for the method as broadly claimed. The Office Action states that the specification is enabling for a method for the diagnosis of first presentation or recurrence of bladder cancer, or a method for diagnosing a urinary infection consisting of detecting a 37 kDa fragment of EGFR in a urine sample, where the fragment is detected using antibody Ab4. The Office Action states that the 37 kDa fragment cannot be detected with any and all antibodies.

Applicants respectfully disagree. Claim 3 has been canceled, and Applicants have amended claims 2 and 10 to recite that the 37 kDa fragment is detected by an antibody that specifically binds the 37 kDa fragment. Applicants respectfully submit that methods of making antibodies that specifically bind to particular protein, or fragments of proteins, are well known. In addition, the specification teaches (and amended claim 4 and new claim 13 recite) that such an antibody can be one that is raised against a peptide corresponding to amino acid residues 1005 to 1016 of EGFR. Applicants therefore submit that the amended claims are fully enabled.

The Office Action also states that claim 10 is not enabled with regard to methods of diagnosing prostate cancer. Claim 10 has been amended and does not cite methods of diagnosing prostate cancer.

Applicants respectfully request that the rejection on this basis be reconsidered and withdrawn.

Claims 4-5 have been rejected under 35 U.S.C. § 112, first paragraph, the Office Action stating that the specification does not provide evidence that the claimed biological materials are

either known and readily available to the public, reproducible from the written description (*e.g.*, sequenced), or deposited.

Claim 5 has been canceled, and claim 4 has been amended to recite that the antibody is raised against a peptide corresponding to amino acid residues 1005 to 1016 of EGFR. New claim 13 uses the same language as amended claim 4, but depends from claim 10.

Applicants respectfully submit that the biological material in question (*i.e.*, the antibody) is reproducible from the written description. The Office Action states that the specification must provide evidence that "the claimed biological materials are . . . reproducible from a written description (e.g. sequenced)". Applicants respectfully submit that those of ordinary skill in the immunological arts do not sequence antibody protein sequences with an intention of then reproducing them by protein synthesis. It is instead far easier to produce the functional antibody proteins by means of injecting the antigen (in this case, the peptide corresponding to amino acid residues 1005 to 1016 of EGFR) into an animal, and then harvesting the antibodies from the serum of the animal. Such methods have been well-known for many years. Applicants respectfully submit that in the case of antibodies, therefore, requiring sequencing of the antibody to show enablement effectively raises the enablement standard for the antibody art above that of other arts.

Antibodies that specifically bind to the 37 kDa fragment of EGFR can be made and tested for their specificity of binding to that fragment. Undue experimentation is not required. Applicants therefore respectfully submit that amended claim 4, and new claim 13, are fully enabled, and respectfully request that the rejection on this basis be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 102(b)

Claims 5, 10 and 12 are rejected under 35 U.S.C. § 102(b) as being anticipated by Ritchie *et al.* (*British J. Cancer* 78(Supp. 1):54(Abstract P118), May 1998) ("Ritchie"). The Office Action states that Ritchie teaches a method for the diagnosis of bladder cancer, and that this method comprises a test for EGFR in a urine sample. The Office Action concludes that claim 10, with its use of "comprising" language, is inherently anticipated by Ritchie, while claim 2, with its use of "consisting" language, is not.

Claims 5 and 12 are canceled, rendering moot the rejection against these claims. Claim 10 has been amended to recite a method that consists of detection of the 37 kDa fragment. Applicants note that Ritchie makes no link between *urinary* EGFR and its use as a diagnostic marker. Ritchie tested (i) urinary EGF levels, (ii) urinary pH and (iii) expression of EGFR by bladder tumors, in patients with bladder cancer. That is, EGFR was assayed by taking formalin-fixed, paraffin embedded tissue from resected bladder tumors, and staining the tissue with EGFR antibody. Ritchie does not show the assaying of EGFR in urine. In contrast, Applicants' claims recite methods of assaying EGFR shed into the urine, not EGF.

Applicants respectfully submit that Ritchie cannot anticipate the subject matter of claim 10, as amended, or new claims 13-19, and respectfully request that the rejection on this basis be reconsidered and withdrawn.

Applicants submit that in view of the foregoing remarks, all issues relevant to patentability raised in the Office Action have been addressed. Applicants respectfully request the withdrawal of rejections over the claims of the present invention. Please apply any charges or credits to Deposit Account No. 50-1721.

Respectfully submitted,

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